Advancing Treatment 2.0: Progress on the 2013 Consolidated Guidelines – What’s new

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Coordinator Treatment and Care

November 5, 2012
Overview

- Major shifts in technical guidance in 2011-2012
- Potential new game changers for 2013 Guidelines
- Timeline of 2013 Consolidated Guideline Process
Scale-up of ART, number of AIDS deaths and new HIV infections in LMIC*, 2001–2011

* LMIC = Low- and middle-income countries
The 15 million target can be achieved

- Blue: Gap based on CD4+ count
- Red: Receiving antiretroviral therapy
- Black: ART coverage

Gap based on the need for treatment for all HIV-positive pregnant women, serodiscordant couples, HIV-positive female sex workers, HIV-positive MSM and HIV-positive IDU's (regardless of CD4+ count)
Scenarios for the incremental expansion of ARV provision to treat and prevent HIV

<table>
<thead>
<tr>
<th>NUMBER OF PEOPLE ELIGIBLE FOR ART</th>
<th>10 mln</th>
<th>18 mln</th>
<th>24 mln</th>
<th>28 mln</th>
<th>34 mln</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CD4 &lt; 200</td>
<td>Recommended until 2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>CD4 &lt; 350</td>
<td>Recommended since 2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>CD4 &lt; 350 + TasP</td>
<td>Recommended in 2012</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>CD4 &lt; 500</td>
<td>Ongoing systematic review of evidence (GRADE review)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>All HIV+</td>
<td>“Test and treat”</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Serodiscordant couples
Pregnant women
Key affected populations
Types of WHO normative guidance

- GRC (Guidelines Review Committee) guidelines
  - Recommendations: clinical, public health or policy
  - Systematic evidence review and GRADE process

- Technical and programmatic updates

- Operational and strategic guidance documents
GRC approved guidelines 2011-2012

- ARV for prevention
  - Couples testing and counseling
  - Oral PrEP for serodiscordant, MSM, transgender

- Key populations
  - MSM and transgender people
  - Viral hepatitis B and C among PWID
  - Sex worker (in finalization)

- TB/HIV
  - Isoniazid preventive therapy for TB/HIV
  - Collaborative policy
CHTC: TasP for serodiscordant couples

First formal WHO TasP guidance

Strongly recommends couples counseling

Recommends offering ART in a serodiscordant couple irrespective of CD4 count

Operational issues are also addressed
2012 Programmatic Updates

**TasP Update**
- Intensify and scale up ART for those with CD4 < 350
- Identify additional opportunities for TasP (“incremental approach”)
  - Recommended for serodiscordant couples
  - Move towards offering ART pregnant women (option B+)
  - Explore feasibility in key affected populations

**eMTCT: Use of ARVs for pregnant women and infants**
- Programmatic implications of options A vs B/B+
- Consideration of life-long ART for pregnant women

Phase-out of Stavudine in national programmes (under development)
TREATMENT 2.0 INITIATIVES
Strategic Use of ARVs – IAC 2012

Using ARVs Strategically and effectively

- Evolving scenarios of earlier ART initiation

- New programmatic updates
  - Pregnant women
  - TasP and PrEP

- Better drugs used more effectively

- Better diagnostics
2012 Technical updates

Three updates on treatment optimization

- Use of efavirenz in pregnancy
- Interchangeability of lamivudine and emtricitabine
- Use of tenofovir in HIV-infected children
ART optimization approaches

**SHORT TERM**
Next 1-2 years

- Improve currently available drugs and formulations
  - Once daily FDC for 1st line (e.g., TDF/3TC/EFV)
  - Heat stable once-daily boosted PI options for 2nd line (e.g., ATV/r)
  - Pediatric formulations (sprinkles, dispersible tablets)

**MEDIUM TERM**
Next 2-5 years

- Add new drugs/better sequencing
  - Replacement of regimen components by new drugs/classes (e.g., integrase inhibitors, NRTI pro-drugs, entry blockers)

**LONG TERM**
Next 5-10 years

- Use new strategies
  - New therapeutic approaches (e.g., induction/maintenance, co-therapies, anti-latency drugs)
## Potential cost benefits of optimizing ARVs

*Adapted from Crawford et al, 2012*

<table>
<thead>
<tr>
<th>ARV drug</th>
<th>Optimization methods</th>
<th>Present cost (per patient/year)</th>
<th>Expected cost (per patient/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF</td>
<td>Process chemistry and dose optimization</td>
<td>87</td>
<td>63 (↓28%)</td>
</tr>
<tr>
<td>AZT</td>
<td>Dose optimization</td>
<td>89</td>
<td>60 (↓33%)</td>
</tr>
<tr>
<td>EFV</td>
<td>Reformulation and dose optimization</td>
<td>63</td>
<td>31 (↓51%)</td>
</tr>
<tr>
<td>ATV/r</td>
<td>Process chemistry and reformulation</td>
<td>355</td>
<td>125 (↓65%)</td>
</tr>
<tr>
<td>DRV/r</td>
<td>Process chemistry dose optimization and reformulation</td>
<td>835</td>
<td>335 (↓60%)</td>
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Expert Meeting Report: SHORT, MEDIUM AND LONGER TERM PRODUCT DEVELOPMENT PRIORITIES IN HIV-RELATED DIAGNOSTICS (June 2012)

- **CD4, VL, EID - Short Term priorities**
  - Market CD4 technologies in the pipeline
  - BlueOcean LG series, FACSClearcount
  - POC testing: BD Biosciences, MBio Diagnostics, Daktari Diagnostics, Omega Diagnostics
  - POC tests for EID
  - Expedite: Liat, Alere NAT, Lynx EID Northwestern Global Health Foundation (NWGF), NWGF VL, SAMBA EID, SAMBA VL

- **CD4, EID, VL - Medium and longer term**
  - POC CD4 & EID tests which are device-free
  - Semi-automated devices for deployment
Breakthroughs in diagnostic testing and patient monitoring at point-of-care

- Point-of-care CD4 is just emerging
  - 3 products available and 1 prequalified
- Point-of-care testing for VL and EID is imminent
- Affordability is key

Number of POC technology releases expected (cumulative numbers)

- CD4
- Viral Load

<table>
<thead>
<tr>
<th>Year</th>
<th>CD4</th>
<th>Viral Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2013</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2014</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Later</td>
<td>6</td>
<td>6</td>
</tr>
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</table>
Pipeline of EID and VL POC Solutions

In the Pipeline for POC VL

CONSOLIDATED GUIDELINES
2013
**Concept for 2013 guidelines**

**WHAT TO DO?**
- HIV Testing
- Pre-ART Care and Prevention
- When to start?
- What to start with?
- How to monitor? (treatment response and toxicity)
- When to switch?
- What to switch to?
- How to monitor?
- Co-infections, co-morbidities and toxicities

**HOW TO DO IT?**
- HIV Testing Approaches
- Linkage to Care
- Adherence/Retention
- Service Integration
- Community Engagement
- De-centralisation
- Task-shifting
- Lab considerations

**HOW TO DECIDE WHAT TO DO, WHERE AND WHEN?**
- Criteria to to inform decision-making (including impact, ethics and cost-effectiveness)
- Decision-making framework/tool for country ART prioritisation
- Guidance on M&E

**ALONG THE CONTINUUM OF HIV CARE**
# Key features of consolidated guidelines

<table>
<thead>
<tr>
<th>KEY FEATURE</th>
<th>SCOPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addressing all ages and populations</td>
<td>Adults, adolescents, children, pregnant women, MARPS (MSM, IDU, sex worker, prisoners)</td>
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<tr>
<td></td>
<td>TB-HIV and HIV-HBV and HCV</td>
</tr>
<tr>
<td>Target audience and approach</td>
<td>Programme managers in RLS, but also concentrated epidemic settings in middle income countries</td>
</tr>
<tr>
<td></td>
<td>Public health approach</td>
</tr>
</tbody>
</table>
Distribution of 2013 WHO Guidelines adult PICO questions along the continuum of HIV care

1. HIV Testing
   - General HIV Care and Prevention
     - Initial assessment
     - Management of co-infections
     - Screening and prophylaxis
     - Prevention in positives
     - Prevention in negatives

2. Initiating ARV
   - When to start?
   - What to start with?

3. Monitoring
   - ARV treatment response
   - Management of toxicities and other complications

4. Changing to ARV 2nd Line
   - When to switch?
   - What to switch to?

5. Changing to ARV 3rd Line

6. Operational and service delivery
   - Adherence
   - Retention
   - Task Shifting
   - Integration
   - De-centralization
   - Community engagement

HIV/AIDS Department

World Health Organization
How the PICOTs / systematic reviews match up

When to start?
- > 350 cells or regardless of CD4
  - All?
  - Pregnant women
  - HIV-HBV/HCV co-infection
    - > 50 years
- Children 2-5 years
- HIV-2

What to start?
1st line (adults and children)
- Use of Tenofovir
- 3TC vs. FTC
- Once daily NNRTI
- EFV in pregnant women

ARV strategies in < 3 yrs
- LPV vs. NVP
- PI sparing
- ARV interruption
- 4 vs. 3 drugs
When to start ART: Some scenarios

Estimated millions of people eligible for ART in LMIC in 2011

11  15  23  25  32

1. CD4 ≤ 200
   - Recommended since 2002

2. CD4 ≤ 350
   - Recommended since 2010
   - + TB/HIV, HBV/HIV

3. CD4 ≤ 350
   - + Expanded CD4 independent conditions

4. CD4 ≤ 500
   - Ongoing systematic review of evidence (GRADE review)

5. All HIV+
   - “Test and treat” (modeling studies)

ART regardless of CD4 count for:
- HIV-serodiscordant couples
- Pregnant women?
- Hepatitis C? HIV-2? Over 50s?
- Key populations (IDU, SW, MSM)?
## Operational systematic reviews

<table>
<thead>
<tr>
<th>Topic area</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community based testing and counselling</td>
<td>- Provision of community HIV testing and counselling (HTC) by non-physician</td>
</tr>
<tr>
<td>Decentralisation</td>
<td>- Provision of ART initiation and maintenance care in community</td>
</tr>
<tr>
<td>Integration</td>
<td>- ART and TB services</td>
</tr>
<tr>
<td></td>
<td>- TB, antenatal and MCH services</td>
</tr>
<tr>
<td></td>
<td>- HIV, TB and drug dependency</td>
</tr>
<tr>
<td>Task-shifting</td>
<td>- ART initiation</td>
</tr>
<tr>
<td></td>
<td>- ART and HIV care maintenance</td>
</tr>
<tr>
<td>Adherence</td>
<td>- E-reminders for promotion of adherence</td>
</tr>
</tbody>
</table>
Programmatic Implications

Generalized Epidemic
- High ART coverage

Concentrated Epidemic
- High ART coverage

Generalized Epidemic
- Low ART coverage

Concentrated Epidemic
- Low ART coverage

- Specific PICOT Questions
9 WHEN TO START?
9.2 HIV-TB CO-INFECTION

BACKGROUND

GUIDING PRINCIPLES

RECOMMENDATIONS

RATIONALE FOR RECOMMENDATIONS
EVIDENCE SUMMARY: www.who.evidencesummary.org.com

OPERATIONAL CONSIDERATIONS FOR PROVIDERS AND SERVICES
- Nam cursus morbi ut minhahnam enim leo egestas id condimentum at laoreet.
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- Mattis massased eleifend nonummy diamassent.
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Timelines

- Modelling meeting for Programmatic guidance
- Results of commissioned systematic reviews
- Preparation of adult and MCH draft recommendations
- Operational GDG meeting 5 – 8 Nov
- Adult and MCH GDG meeting 10 – 13 Dec
- Programmatic GDG meeting Jan 15-17
- Core Coordinating Guidelines meeting
- GDG and Peer Review
- Finalisation of draft guidelines
- Publication Process

September

October

November

December

January

February

March

April

May

June
Summary

- Many changes in 2011-12

- More changes likely in 2013 – currently undergoing systematic reviews and GRADE evaluation

- Trend toward earlier initiation; will include recommendations for key populations

- VL use will be increasingly important

- With strategic use of ARVs, increasing access to ART and scale-up, can reach 15 million on ART by 2015